

Weight Loss in Type 2 Diabetic Patients

A guiding principle in the treatment of type 2 diabetic patients has been the recommendation to lose weight (1,2). This is because the health benefits of weight loss have long been recognized (3). As weight loss progresses and is maintained, an improvement of glycemia may be evidenced by a reduction in glycosylated hemoglobin (4,5).

Redmon et al. (6) report in this issue of *Diabetes Care* the 2-year outcome of a combination of weight loss therapies in type 2 diabetic patients. The end result was a weight loss of 4.6 kg sustained over 2 years, which led to a decrease of HbA_{1c} of 0.5%. While full credit must be given to the authors for their innovative approach, and for their hard and dedicated work, it is disappointing that such a combination therapy program in an excellent medical center with outstanding clinicians and facilities could not lead to a greater weight loss and particularly a greater improvement in blood glucose control.

Why is weight loss in obese diabetic patients so modest? Here, as mentioned, in the best of hands, patients who started at a weight of 113.2 kg ended 2 years later at a weight of 108.6, a 4% drop. Why can't we do better, all of us, in treating type 2 diabetic patients?

Therapeutic weight loss in type 2 diabetic patients has been very difficult to achieve. In an 18-month study that compared the use of three sets of dietary guidelines for type 2 diabetes (7), no significant changes in body weight were observed. Diabetologists have often ignored standards of care indicating that lifestyle change with diet and exercise be the initial intervention because of their belief that this is an exercise in futility. Weight loss for anyone is difficult. For type 2 diabetic patients, it has been particularly so. Why?

One reason is energy expenditure, which is lowered with adequate treatment. Diabetic patients who are not in good control tend to have an energy expenditure that is more elevated than would be predicted for their weight and age. This is because diabetic patients in poor control show an increased protein turnover, requiring an increased protein

synthesis, which is thermogenically expensive. After treatment and an improvement in glucose control, this protein catabolic effect decreases and energy expenditure drops toward normal (8,9). There have been reports that obese patients have an increased sympathetic tone, which increases thermogenesis. As weight is lost, this thermogenic effect decreases.

Also, as diabetes control improves with caloric restriction, urinary glucose decreases or disappears altogether, leading to a decreased excretion of calories in the urine. This increased caloric retention will lead to decelerating weight or to weight regain if caloric intake does not drop further.

In addition, there is the direct effect of weight loss. Energy expenditure begins to drop as soon as weight begins to decrease in obese individuals (10,11). Thus, a reactive metabolic response occurs as soon as an individual begins to lose weight. Also, as weight is lost, not only is resting metabolic rate decreased, but nonresting energy expenditure is also less because less mass is being moved around, requiring less effort to carry it (12,13). There is also a powerful force to eat more, again in an effort to prevent further weight loss.

Weight loss trials in diabetic patients are quite consistent. People lose weight over 4–6 months and then see their weight plateau (in the present report, the plateau occurred at 10 months, probably due to the more comprehensive strategy used). People generally lose from ~4 to 10% from baseline weight and then stop. At this point, they have reached a new equilibrium between their decreased caloric intake and their energy expenditure. Hypothalamic signals in defense of body weight have increased and intervene to prevent further weight loss. In fact, the orexigenic stimuli initiate a regain of weight that almost inexorably occurs. The powerful drive to regain the weight is due to an imprinting in an individual's hypothalamic centers of a "defensible body weight," and this is at the pre-weight-loss weight. The orexigenic neurotransmitters important in driving food intake are activated to such an extent that the signal lev-

els become very difficult to ignore. Hunger increases, satiety decreases, and a return to the old "equilibrium" occurs.

Besides the biological "reasons" for a poor response, is the resistance to weight decrease greater in diabetic than in non-diabetic individuals also because of psychological reasons? What is it about type 2 diabetes that seems to inhibit weight loss success? Possibly, there is fatigue from a long history of weight loss intervention attempts that have failed. With frequent relapses there is often a feeling of failure, frustration, depression, and anger (14,15). This can lead to a sense of hopelessness and powerlessness that vitiates further success. It must be emphasized that the primary agent for change is the patient and not the physician. Thus, the initial requirement for greater success is a motivated patient who will actively pursue a very difficult course, rather than a passive one who expects to be "treated."

There is the important question of the adequacy of the behavioral modification program. Behavior modification begins with education. Some nutritional knowledge is necessary to place behavior in context. Many programs avoid this or do not do this well. As a result, the patient is not appropriately aware of the changes required to achieve and maintain weight loss. This seems to have been well done in the Redmon study. After and during this education, however, certain behavioral strategies are very important. These include self-monitoring, stimulus control, contingency management, stress management, modeling, social support, and cognitive approaches (16).

Obese patients are generally very sedentary and find it difficult to increase exercise. Diabetic patients with neuropathy, foot ulcers, heart disease, or other complications have a particularly difficult time. Thus, attempts at increasing exercise are often unsuccessful. Special attention to appropriate physical activity, given diabetes complications, is crucial if an increase in physical activity is to be achieved.

Also, most diabetic patients are on antidiabetic medication. Weight gain with such pharmacotherapy is common and

can be quite large. The U.K. Prospective Diabetes Study showed that after an initial weight loss with dietary instruction, type 2 diabetic patients showed a gradual but impressive weight gain over a period of 15 years of treatment with drugs (17). With new standards of care that are setting lower HbA_{1c} levels, more medications are used that enhance anabolism and weight gain. These medications include sulfonylureas, meglitinides, insulin, and thiazolidinediones. Thus, the effort to drive HbA_{1c} down to prevent complications clashes with the effort to lower weight.

The approach with regard to weight loss in diabetic patients will need to be more aggressive. A program requires more than educational sessions with dietitians and a manual of instruction on weight loss, as was done here. Behavioral change requires a more engaged and intensive program. This was successful in the Diabetes Prevention Program (18) in prediabetic patients and is now being tried in the LookAHEAD trial with diabetic patients (19).

Also, further research is needed, as was done in the Redmon study, to investigate ways to increase the amount of weight loss attainable with current treatment modalities and to facilitate long-term weight loss maintenance.

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